

PSJ14 Janssen Opp Exh 17 – JAN-MS-02320051

ANALGESIA TACTICAL PLAN

US MEDICAL AFFAIRS

MARCH 2014

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ONE TEAM Making the Difference for Patients WORLDWIDE



Strategic Imperatives & Strategic Drivers

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GROW within targeted universe

- Drive **awareness** and **educate** on appropriate use to increase product **adoption**
- Improve **effectiveness** of PAIN FORCE and Inside Sales Team
- Continue **patient savings** program
- **Enhance peer-to-peer education** content & vehicle
- Evolve commercial presence to **deliver greater local impact**
- **Supplement selling efforts** with focused non-personal tactics
- Capitalize on **specific payer channels** in **select geographies**

\$7.4MM (83%)

PROTECT access to our products

- **Increase payer engagement** in anticipation of market events
- Explore **alternate** distribution **channels**
- **Engage external stakeholders** to improve product access at pharmacy
- **Support HCP and pharmacy partnership** to help patients get prescriptions filled
- Anticipate and address **policy** changes to enable appropriate access to medications

\$1.4MM (17%)

COMMUNICATE differentiating evidence

- Support **regulatory and compliance** requirements
- **Strengthen insights and scientific exchange** through external engagement
- **Enhance value prop** by generating and disseminating clinical and economic data

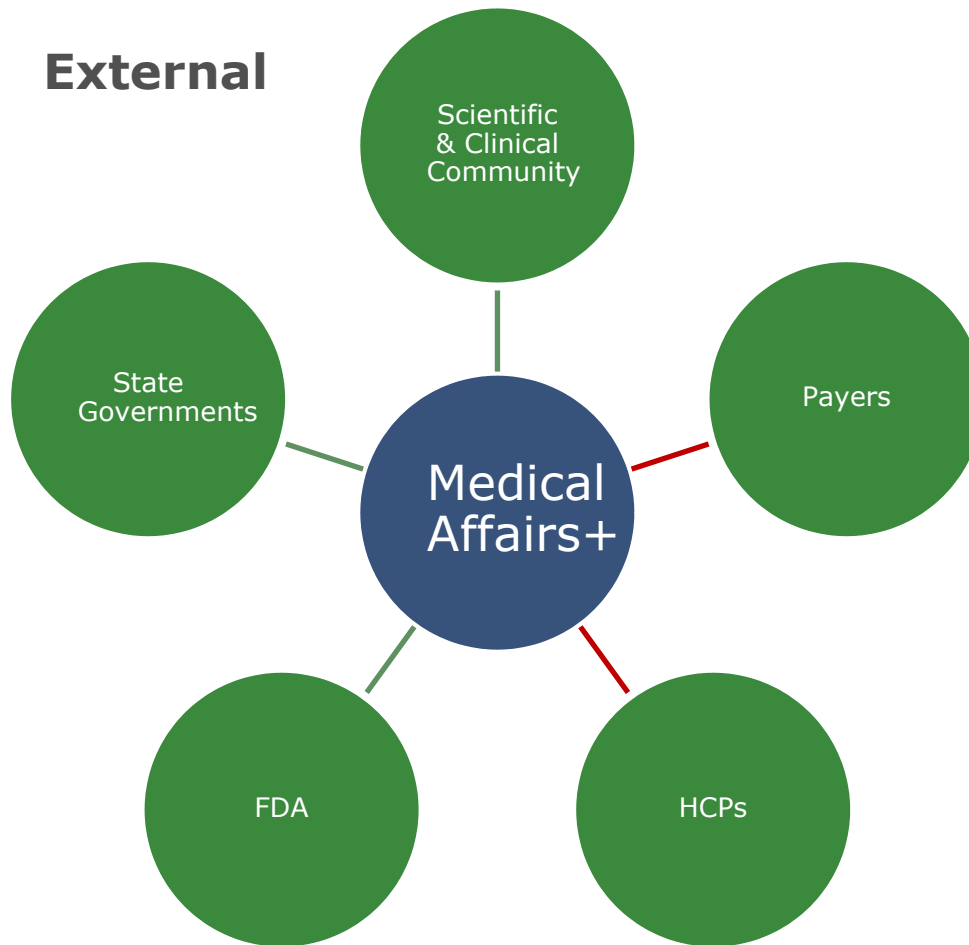
\$5.0MM

\$8.8MM Total BMEs (100%)

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OUR PARTNERS

External



Internal



*All interactions in accordance with *Guidance Document on the Promotion of FDA-Regulated Products and the Dissemination of Scientific Information* (dated 09/10/2012)

FDA POST MARKETING REQUIREMENTS

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BACKGROUND

FDA requested NDA holders of branded LAOs to conduct 4 PMR Observational studies (abuse/misuse and diversion) and 1 clinical study (hyperalgesia).

OBJECTIVE:

Dr. Shopping Study: To define and validate “doctor/pharmacy shopping” as outcomes suggestive of abuse, misuse and/or addiction

Hyperalgesia: To assess the risk/benefit (hyperalgesia) of long term treatment in patients with chronic pain, especially patients with poor response to opioid treatment

DESIGN:

Dr. Shopping: A retrospective cohort study to assess incidence of Dr. Shopping from databases and medical records.

Hyperalgesia: 27-week multicenter, randomized, double-blind, placebo-controlled study.

TIME & COST:

See Next Slides

LIMITATIONS:

Challenges working in a consortium environment with decision making/



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Analgesia PMR Studies & Advisory Board Meeting Budget Information



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FDA PMR Studies Estimated Costs

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Study Number	Number of Subjects	Total Costs*/ Janssen Costs (based on 9 sponsors dividing costs)**	Campbell Alliance Project Management Costs	Other (Total Costs/Janssen Costs)
1a) Estimate the incidence of misuse, abuse, addiction, overdose and death associated with long term use of opioids for chronic pain	~10,000 (~5K/subject)	50M*/ 5.5M**	~600K/year x 4 years	<ul style="list-style-type: none"> Advisors: 1.2M / 150K Meetings: 1.28M /160K (~6 meetings/year over 4 years) Filing Fees: TBD Publications: 600K /75
1b) Evaluate and quantify other risk factors for misuse, abuse, addiction, overdose and death associated with long term use of opioids for chronic pain	Claims Database review	1M* /111K**		
2) Develop and validate measures of opioid related adverse events used to design PMR 1	NA	8M*/900K**		
3) Validate coded medical terminologies used to identify opioid related adverse events used to design PMR 1	~10,000 charts	10M* /1.11 M**		
4) Define and validate "doctor/pharmacy" shopping as outcomes suggestive of misuse, abuse and addition.	—	—		
4a) Claims Database review	NA	1M* /112 K**		
4b) Subject Survey	~15,000	4M* /450K**		
5) Clinical trial to estimate the serious risk for the development of <u>hyperalgesia</u>	2,000 (~40K/subject)	80M* /9 M**		
Total		154M*/ 17.2M**	2.4M*/ 270K**	3.1M*/ 350K**

Total = 167M / 171M

FDA PMR Timelines

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FDA Timelines			
Study	Final Protocol Submission to FDA	Study Completion	Final Report Submission to FDA
1	8/20/2014	01/2018	06/2018
2	08/2014	08/2015	11/2015
3			
4			
5	8/2014	8/2016	2/2017



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Estimated Cost Breakdown

Estimated Total Costs By Year					
	2014	2015	2016	2017	2018
Study1 a/b	200K	800K	21 M	20 M	8 M
Study 2	8 M	15 M			
Study 3					
Study 4					
Study 5	2M	25M	25M	20M	8M
Campbell	600K	600K	600K	600K	300K
Other	1.25K	1.4 M	150K	150K	150K
Total	110M*/1.2M*	50M*/6M**	47M*/5.2M**	41M*/4.6M**	1.65M*/2M**

*Total Costs

** Janssen Costs (Based on total divided among 9 NDA Holders)



FMRI STUDY

BACKGROUND:

Tapentadol is a opioid with dual action mechanism of both opioid-mu receptor and norepinephrine modulations. fMRI is an idea tool to assess the brain activity changes caused by the treatment of Tapentadol.

OBJECTIVE:

- Correlation of brain activity changes and the pain relief efficacy of Tapentadol ER in chronic low back pain patients.
- Assessing the brain activity in the region related to mood changes and psychological behavior between the treatment of Tapentadol ER and placebo.

DESIGN

- This is a pilot phase IV study with randomized, double blind, placebo control, repeated dose treatment design to assess the correlation of brain activity changes and the pain relief efficacy of Tapentadol ER vs. placebo in chronic low back pain patients.

TIME & COST:

- Study completion: Sept. 2015
- CSR: Dec. 2015
- Cost: \$200K for 2014 and \$300K for 2015.

LIMITATIONS:

This study will assess the BOLD signal using fMRI to indirectly measure the brain activity changes. BOLD signal comes with other false positive signals.

ABUSE DATA-RESEARCHED ABUSE, DIVERSION AND ADDICTION-RELATED SURVEILLANCE (RADARS) SYSTEM

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BACKGROUND:

The RADARS System measures rates of prescription opioid abuse and diversion throughout the US. The RADARS System is composed of several programs : drug diversion, survey of key informants' patients, poison control centers, opioid treatment centers, and college survey

OBJECTIVE:

Monitor the abuse, misuse and diversion profile of tapentadol

DESIGN

Collects the data through surveys
Rates are calculated by population (per 100,000 population) and by Unique Recipients of Dispensed Drugs (per 1,000 URDD).

TIME & COST:

- Quarterly reports
- \$ 1.2 million/year

LIMITATIONS:

inherent limitations of data analysis in some of the RADARS programs



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ABUSE NATIONAL ADDICTIONS VIGILANCE INTERVENTION AND PREVENTION PROGRAM (NAVIPPRO®)

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BACKGROUND:

The NAVIPPRO surveillance report for presents data from the Addiction Severity Index Multimedia Version (ASI-MV®), Comprehensive Health Assessment for Teens (CHAT®), and the Web Informed Services (WIS®) Internet Monitoring archive.

OBJECTIVE:

Monitor the abuse, misuse and diversion profile of tapentadol

Collects the data through surveys and internet monitoring

DESIGN

Rates are calculated per 100,000 prescriptions, 100 ASI-MV assessments and per 100

prescription opioid abusers assessed. Internet monitoring posts are analyzed qualitatively

as well as quantitatively

TIME & COST:

- 3 reports/year
- \$ 1.0 million/year

LIMITATIONS:

Limited data collection



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Title	Status	Est. Pub Submission Timeline
Drug Diversion Analyses of RADARS database (RADARS® System Drug Diversion and Street Rx) - publication to examine diversion and street price of TAP.	1 st draft = April 2014	3Q'2014
Abuse of Long-Acting Opioid Analgesics: Focus on Tapentadol	Draft 2 complete 7/2013; On Hold	TBD
WHO Paper: Tapentadol Clinical Profile and Abuse Risk	On Hold	Internal Use
Comprehensive Review efficacy-tolerability-abuse data	Planning Stage/On Hold	TBD
Assessing abuse potential of new analgesic medications following market release: An evaluation of Internet discussion of tapentadol abuse (WIS)	Complete	12/2013
Tapentadol abuse potential: A post-marketing evaluation using a sample of individuals evaluated for substance abuse treatment (ASI-IV)	Complete	12/20/13
Tamper-Resistant Properties of Tapentadol Extended-Release Tablets: In Vitro Laboratory Analyses	complete	Submitted: 9/2013/ Accepted: 2/2014

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Dose Conversion



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NUCYNTA ER DOSE CONVERSION REVIEW ARTICLE

BACKGROUND:

- Lack of data on how to convert patients from other opioids to Nucynta ER
- Absence of robust conversion data led third-parties to make widely varying assumptions and recommendations

OBJECTIVE:

- To identify and collate available information on patient experience when directly converted to Nucynta ER from Morphine or Oxycodone
- To publish credible source of information on direct conversion to Nucynta ER
- **Use as a commercial material to provide to customer**

DESIGN:

- Review article in development in collaboration with JSA, GMA, CDT, and GRT (poster at International Conference on Opioids in June, manuscript submission in July)
- Utilize Grunenthal (KF-43 & KF-45) and Janssen cancer trial (02) data

TIME & COST:

Timing – 2013-2014

Budget (est*)

Kick-off	1 st Draft	PRC Review	Submit to J	Pub (final)	2013	2014	2015	Total
3/2013	9/2013	2/2014	TBD	TBD	\$50,000 (from pubs)			\$50,000

LIMITATIONS:

- No data converting from hydrocodone
- Existing data from secondary analyses
- Lack of US data

NUCYNTA ER DOSE CONVERSION

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- FDA requested an sNDA to support dose conversion recommendations (3/23/2014)
- Discussions in progress to discuss funding for sNDA
- Costs = ~1M

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Cognition/Mood/Withdraw

COGNITION/MOOD/WITHDRAWAL PUBLICATIONS PLAN 2014

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Title	Status	Est. Pub Submission Timeline
Hypothesis testing of the Potential Differences in Withdrawal, Tolerance and Abuse of Tapentadol Compared to Pure Mu Opioid Agonists: Does Noradrenergic Activity Play a Role?	2/6/14: In development	Q3'2014
Review the available clinical and nonclinical evidence for short or long term AE's of opioids on cognition and discuss the need for studies/methods to better assess the extent to which effects on cognition may be clinically significant	Kick-off: 2/21/14	Q4'2014
Short and long term adverse effects of opioid agonism on mood and the potential for serotonergic and noradrenergic activity to mitigate the effects	Kick-off: 2/21/14	Q4'2014

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Scientific, Clinical Presence & Customer Insight



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Scheduling change options for Tapentadol

BACKGROUND:

Tap scheduling was based on pharmacology, preclinical and clinical data. Real world data consistently showing low rates of abuse, misuse and diversion of tap. It is of interest to get a feedback from the experts in the field on scheduling change options for Tap

OBJECTIVE:

- Review and assess findings of the previous tap Abuse Liability Ad Board Meeting (2010)
- Evaluate tap abuse liability and related studies conducted over the last four years;
- Identify potential data gaps and future studies in order to revise the tap 8-Factor Analysis

DESIGN

- 6-8 KOL with expertise in opioid pharmacotherapy; abuse, and scheduling
- Janssen representatives to present tap data
- Interactive Forum representative/Nat Katz to moderate
- Final report generated outlining the meeting to be developed by Interactive Forum

TIME & COST:

- September 2014
- \$106,708

LIMITATIONS:

- NA

FMRI

BACKGROUND:

Tapentadol is a opioid with dual action mechanism of both opioid-mu receptor and norepinephrine modulations. fMRI is an idea tool to assess the brain activity changes caused by the treatment of Tapentadol.

OBJECTIVE:

- Correlation of brain activity changes and the pain relief efficacy of Tapentadol ER in chronic low back pain patients.
- Assessing the brain activity in the region related to mood changes and psychological behavior between the treatment of Tapentadol ER and placebo.

DESIGN

- This is a pilot phase IV study with randomized, double blind, placebo control, repeated dose treatment design to assess the correlation of brain activity changes and the pain relief efficacy and mood changes after the treatment of Tapentadol ER vs. placebo in chronic low back pain patients.

TIME & COST:

- \$100 K

LIMITATIONS:

This study will assess the BOLD signal using fMRI to indirectly measure the brain activity changes. BOLD signal comes with other false positive signals.

NURSE PRACTITIONER AD BOARD

BACKGROUND:

Nurse Practitioners are playing an increasingly important role in the field of pain management. The MA team would like to develop relationships and engage these external partners by identifying how MA can support and enhance their clinical practice.

OBJECTIVE:

- Evaluate current and future clinical practice and unmet needs for pain management
- Identify knowledge gaps in the current literature and new data analyses and studies that could be used to fill those gaps
- Discuss how knowledge on new products is obtained and evaluate opportunities for disseminating scientific information.

DESIGN

- 8-10 Nurse Practitioners identified as Key Opinion Leaders in the area of pain management
- Janssen representatives to present Nucynta/Nucynta ER data
- Interactive Forum representative to moderate
- Final report generated outlining the meeting to be developed by

TIME & COST:

- Q2'2014
- \$93K

LIMITATIONS:

No precedent for identifying NP Leaders



QUALITY MEASURES AD BOARD

BACKGROUND:

- There is a need to better patient outcomes and define quality measures in the area of pain management/opioid therapy.

OBJECTIVE:

- Discuss Janssen's stance on quality measures and obtain input towards the design of these measures
- Identify strategies on how identified quality measures can be endorsed by the public

DESIGN

- **8-10 Expert Advisors to participate; Expertise may be in managed care; Health Outcomes and HCPs**
- **Moderator TBD**
- **Final report to be generated by vendor**

TIME & COST:

- Q4'2014
- ~\$100K

LIMITATIONS:

- Limited work in the field of quality measures for opioid therapies

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Medical Congresses



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Poster Presentation

Title	Submission Date	Congress/Date
RADARS Street Rx - Drug Diversion 1 - Street Price Lower than Sched II Opioids	Dec 2014	CPDD College on Problems of Drug Depend/ June 2014
RADARS Street Rx - Drug Diversion 2 - Role of TAP-ER in Illicit Mkt	Nov 2013	American Pain Society/ April 2014
RADARS Street Rx - Drug Diversion 3	July 2014	Pain Week/Sept 2014
Opioid Withdrawal & Dependency	TBD	Pain Week/Sept 2014
Opioid - Cognition (short and long-term effects, pre-clin data)		
Opioid - Mood		
Osteoporosis		
Inflexxions Data 1	ASI-IV/WIS	Pain Week/Set 2014
Integrated Risk Benefit	Jan 2014	AMCP Acad Mngd Care Pharm/ April 2014
NNT-Effic of Analgesics	Jan 2014	AMCP Acad Mngd Care Pharm / April 2014